

AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [020] with the following rewritten paragraph:

[0020] In a further aspect, the present invention provides MRI agent compositions and methods for using the compositions, in which substituent X_1 is $-(CH_2CO)-$, n equals 2 and Y_1 is $-Pro-Met-$, m equals 3 and Y_2 is $-Trp-Met-Arg$ (SEQ ID NO:1), and p equals 0.

Please replace paragraph [021] with the following rewritten paragraph:

[0021] In another aspect, the present invention provides MRI agent compositions and methods for using the compositions, in which substituent X_1 is $-(CH_2CO)-$, n equals 1 and Y_1 is $-Met-$, m equals 3 and Y_2 is $-Trp-Met-Arg$ (SEQ ID NO:2), and p equals 0.

Please replace paragraph [022] with the following rewritten paragraph:

[0022] In yet another aspect, the present invention provides MRI agent compositions and methods for using the compositions, in which substituent X_1 is $-(CH_2CO)-$, n equals 0, m equals 3 and Y_2 is $-Trp-Met-Arg$, and p equals 0 (SEQ ID NO:3).

Please replace paragraph [0110] with the following rewritten paragraph:

[0110] Suitable peptide substrates for MMPs include the peptide sequence $Pro-Met-Ala-Leu-Trp-Met-Arg$ (SEQ ID NO:4) (Netzel-Amett, S., et al., 1993, Biochem., 32: 6427-6432). Recognition of the peptide sequence by an MMP can result in cleavage of the peptide sequence $Pro-Met-Ala-Leu-Trp-Met-Arg$ (SEQ ID NO:4) to yield two peptide fragments: $-Pro-Met-Ala-$ and $-Leu-Trp-Met-Arg$ (SEQ ID NO:5). Preferred peptide substrates include $-Ala-Leu-$. Accordingly, TAAGMs can be designed that are peptide substrates for MMPs having the formula:

Please replace paragraph [0120] with the following rewritten paragraph:

[0120] In one specific embodiment of the present invention, X_1 is $-(CH_2CO)-$, n equals 2 and Y_1 is $-Pro-Met-$, m equals 3 and Y_2 is $-Trp-Met-Arg$ (SEQ ID NO:1), and p equals 0.

Please replace paragraph [0121] with the following rewritten paragraph:

[0121] In another specific embodiment of the present invention, X_1 is $-(CH_2CO)-$, n equals 1 and Y_1 is $-Met-$, m equals 3 and Y_2 is $-Trp-Met-Arg$ (SEQ ID NO:2), and p equals 0.

Please replace paragraph [0122] with the following rewritten paragraph:

[0122] In yet another specific embodiment of the present invention, X_1 is $-(CH_2CO)-$, n equals 0, m equals 3 and Y_2 is $-Trp-Met-Arg$ (SEQ ID NO:3), and p equals 0.

Please replace paragraph [0124] with the following rewritten paragraph:

[0124] There are a number of other MMP inhibitors and substrates that can be used. The substrates are particularly useful as cancer cleavage sites with the use of coordination site barriers. These MMP inhibitors and substrates include, but are not limited to, 1, 10-phenanthroline; CT 1847; AG3319, AG3340 (also called Prinomastat), AG3287, AG3293, AG3294, AG3296; 2-mercaptoacetyl L-phenyl-alanyl-L-leucine; $\text{HSCH}_2\text{CH}[\text{CH}_2\text{CH}(\text{CH}_3)_2]\text{CO}-\text{Phe-Ala-NH}_2$; OPB-3206; Furin Inhibitor; 3,4-dihydro-1-oxo-1,2,3-benzotriazine-3-(3-tetrahydrofuryl)-carbonate (1W-1); 1,2-dihydro-3,6-dioxo-2-phenyl-pyridazine-1-methylcarbonate (1W-2); 3,4-dihydro-1-oxo-1,2,3-benzotriazine-3-(2-methoxy) ethylcarbonate (1W-3); 1,2-dihydro-2-ethoxycarbonyl-(1-oxo-isochinolin-5-yl) ethylcarbonate (1W-4); 1(2H)-phthalazinone-2-(4-methoxyphenyl) carbonate (1W-5); N-[2(R)-2-(hydroxamido carbonylmethyl)-4-methyl pentanoyl]-L-tryptophan methylamide also called GM6001, Galardin and ilomastat; BAY 12-9566; Neovastat (AE-941); BB-1101; G1129471; $\text{Ph}(\text{CH}_2\text{NH-D-R}_{\text{res}}\text{CO}-\text{CH}_2\text{CH}_2\text{D})_2$; also called FC-336; Mca-Pro-Leu-Gly-Leu-Dpa-Ala-Arg-NH₂ (SEQ ID NO:6) (cleavage occurs between Gly and Leu); DNP-Pro-Leu-Gly-Ile-Ala-Gly-Arg-000H (SEQ ID NO:7) (cleavage occurs between Gly and Leu); arboxymethyl transferrin (Cm-Tf); (7-methoxycoumarin-4-yl)acetyl-1-PLGP (SEQ ID NO:21)-[3-(2,4-dinitrophenyl)-L-2,3 diaminopropionyl]-AR-NH₂; (7-methoxycoumarin-4-yl)acetyl-PLAQAV (SEQ ID NO:22)-[3-(2,4-dinitrophenyl)-L-2,3 diaminopropionyl]-RSSSR (SEQ ID NO:23)-NH₂; Ac-PLG-[2-mercapto-4-methylpentanoyl]-L-G-OEt; Peptide I: GPLGLRSW (SEQ ID NO:24); and Peptide II: GPLPLRSW (SEQ ID NO:25). See generally, Greenwald, R. A. et al. In vitro sensitivity of the three mammalian collagenases to tetracycline inhibition: relationship to bone and cartilage degradation. *Bone* 22, 33-38 (1998); Kolb, S. A. et al. Matrix metalloproteinases and tissue inhibitors of metalloproteinases in viral meningitis: upregulation of MMP-9 and TIMP-1 in cerebrospinal fluid. *J. Neuroimmunol.* 84, 143-150 (1998); Charoenrat, P. et al. Overexpression of epidermal growth factor receptor in human head and neck squamous carcinoma cell lines correlates with matrix metalloproteinase-9 expression and in vitro invasion. *Int. J. Cancer* 86, 307-317 (2000); Uzui, H., Lee, J. D., Shimizu, H., Tsutani, H. & Ueda, T. The role of protein-tyrosine phosphorylation and gelatinase production in the migration and proliferation of smooth muscle cells. *Atherosclerosis* 149, 51-59 (2000); Montesano, R., Soriano, J. V., Hosseini, G., Pepper, M. S. & Schramek, H. Constitutively active mitogen-activated protein kinase MEK1 disrupts morphogenesis and induces an invasive phenotype in Madin-

Darby canine kidney epithelial cells. *Cell Growth Differ.* 10, 317-332 (1999); Yip, D., Ahmad, A., Karapetis, C. S., Hawkins, C. A. & Harper, P. G. Matrix metalloproteinase inhibitors: applications in oncology. *Invest New Drugs* 17, 387-399 (1999); Price, A. et al. Marked inhibition of tumor growth in a malignant glioma tumor model by a novel synthetic matrix metalloproteinase inhibitor AG3340. *Clin. Cancer Res.* 5, 845-854 (1999); Santos, O., McDermott, C. D., Daniels, R. G. & Appelt, K. Rodent pharmacokinetic and anti-tumor efficacy studies with a series of synthetic inhibitors of matrix metalloproteinases. *Clin. Exp. Metastasis* 15, 499-508 (1997); Barletta, J. P. et al. Inhibition of pseudomonal ulceration in rabbit corneas by a synthetic matrix metalloproteinase inhibitor. *Invest Ophthalmol. Vis. Sci.* 37, 20-28 (1996); Maquoi, E. et al. Inhibition of matrix metalloproteinase 2 maturation and HT1080 invasiveness by a synthetic furin inhibitor. *FEBS Lett.* 424, 262-266 (1998); Makela, M. et al. Matrix metalloproteinase 2 (gelatinase A) is related to migration of keratinocytes. *Exp. Cell Res.* 251, 67-78 (1999); Hao, J. L. et al. Effect of galardin on collagen degradation by *Pseudomonas aeruginosa*. *Exp. Eye Res.* 69, 595-601 (1999); Hao, J. L. et al. Galardin inhibits collagen degradation by rabbit keratocytes by inhibiting the activation of pro-matrix metalloproteinases. *Exp. Eye Res.* 68, 565-572 (1999); Wallace, G. R. et al. The matrix metalloproteinase inhibitor BB-1 101 prevents experimental autoimmune uveoretinitis (EAU). *Clin. Exp. Immunol.* 118, 364-370 (1999); Maquoi, E. et al. Membrane type 1 matrix metalloproteinase-associated degradation of tissue inhibitor of metalloproteinase 2 in human tumor cell lines: *J. Biol. Chem.* 275, 11368-11378 (2000); Ikeda, T. et al. Anti-invasive activity of synthetic serine protease inhibitors and its combined effect with a matrix metalloproteinase inhibitor. *Anticancer Res.* 18, 4259-4265 (1998); Schultz, S. et al. Treatment of alkali-injured rabbit corneas with a synthetic inhibitor of matrix metalloproteinases. *Invest Ophthalmol. Vis. Sci.* 33, 3325-3331 (1992); Buchardt, J. et al. Phosphinic Peptide Matrix Metalloproteinase-9 Inhibitors by Solid-Phase Synthesis Using a Building Block Approach. *Chem. Eur. J.* 5, 2877-2884 (2000); Dahlberg, L. et al. Selective enhancement of collagenase-mediated cleavage of resident type II collagen in cultured osteoarthritic cartilage and arrest with a synthetic inhibitor that spares collagenase 1 (matrix metalloproteinase 1). *Arthritis Rheum.* 43, 673-682 (2000); Lombard, M. A. et al. Synthetic matrix metalloproteinase inhibitors and tissue inhibitor of metalloproteinase (TIMP)-2, but not TIMP-1, inhibit shedding of tumor necrosis factor-alpha receptors in a human colon adenocarcinoma (Colo 205) cell line. *Cancer Res.* 58, 4001-4007 (1998); Lein, M. et al. Synthetic inhibitor of matrix

metalloproteinases (batimastat) reduces prostate cancer growth in an orthotopic rat model. *Prostate* 43, 77-82 (2000); Brown, P. D. Matrix metalloproteinase inhibitors in the treatment of cancer. *Med. Oncol.* 14, 1-10 (1997); Garbett, E. A., Reed, M. W. & Brown, N. J. Proteolysis in colorectal cancer. *Mol. Pathol.* 52, 140-145 (1999); Itoh, M. et al. Purification and refolding of recombinant human proMMP-7 (pro-matrilysin) expressed in *Escherichia coli* and its characterization. *J. Biochem. (Tokyo)* 119, 667673 (1996); Wang, Y., Johnson, A. R., Ye, Q.Z. & Dyer, R. D. Catalytic activities and substrate specificity of the human membrane type 4 matrix metalloproteinase catalytic domain. *J. Biol. Chem.* 274, 3304333049 (1999); Ohkubo, S. et al. Identification of substrate sequences for membrane type-1 matrix metalloproteinase using bacteriophage peptide display library. *Biochem. Biophys. Res. Commun.* 266, 308-313 (1999), all of which are expressly incorporated by reference; the structures of some of these are shown in FIG. 7.

Please replace paragraph [0136] with the following rewritten paragraph:

[0136] In a preferred embodiment, the TAAGM is involved in angiogenesis. There are a wide variety of moieties known to be involved in angiogenesis, including, but not limited to, vascular endothelial growth factors (VEGF; including VEGF-A, VEGF-B, VEGF-C and VEGF-D), FGF-1 (aFGF), FGF-2 (bFGF), FGF-3, FGF-4, hepatocyte growth factor (HGF, scatter factor), thymidine phosphorylase, angiogenin, IL-8, TNF- α , leptin, transforming growth factors (TGF- α , TGF- β), platelet-derived growth factor, proliferin, and granulocyte colony stimulating factor (G-CSF). Known angiogenesis inhibitors include, but are not limited to, platelet factor 4, thrombospondin-1, interferons (IFN- α , IFN- β , IFN- γ), IL-1, IL-2, vascular endothelial growth inhibitor (VEGI), 2-methoxyestradiol, tissue inhibitors of MMPs (TIMPs), proliferin related protein, angiostatin, endostatin, amion terminal fragment of u-PA (ATF), thalidomide, TNP-470/AGM-1470, carboxyamidotriazole, maspin, AG3340, marimastat, BAY9566, CSG-27023A, gly-arg-gly-asp-ser (GRGDS) (SEQ ID NO:8), tyr-ile-gly-ser-arg (YIGSR) (SEQ ID NO:9) and ser-ile-lys-val-ala-val (SIKVAV) (SEQ ID NO:10). See van Hinsbergh et al, *Annals of Oncology* 10 Supp. 4:60 (1999) and references therein; Li et al., *Human Gene Therapy* 10(18):3045 (1999); Duenas et al., *Investigative Ophthalmology*, 1999; Bauer et al., *J. Pharmacology & Experimental Therapeutics* 292(1):31 (2000); Zhang et al., *Nature Medicine* 6(2):196 (2000); Sipose et al., *Annal of the New York Academy of Sciences* 732:263 (1994 and references therein); Niresia et al,

Am. J. Pathology 138(4):829 (1991); Yamamura et al., Seminars in Cancer Biology 4(4):259 (1993).

Please replace paragraph [0194] with the following rewritten paragraph:

[0194] In a preferred embodiment, the targeting moiety is a nuclear localization signal (NLS). NLSs are generally short, positively charged (basic) domains that serve to direct the moiety to which they are attached to the cell's nucleus. Numerous NLS amino acid sequences have been reported including single basic NLS's such as that of the SV40 (monkey virus) large T Antigen (Pro Lys Lys Lys Arg Lys Val) ([SEQ ID NO:11](#)). Kalderon (1984), et al., Cell, 39:499-509; the human retinoic acid receptor- β nuclear localization signal (ARRRRP) ([SEQ ID NO:12](#)); NFkB p50 (EEVQRKRQKL ([SEQ ID NO:13](#)); Ghosh et al., Cell 62:1019 (1990); NFkB p65 (EEKRKRTYE ([SEQ ID NO:14](#)); Nolan et al., Cell 64:961 (1991); and others (see for example Bouliskas, J. Cell. Biochem. 55(1):32-58 (1994), hereby incorporated by reference) and double basic NLS's exemplified by that of the Xenopus (African clawed toad) protein, nucleoplasmin (Ala Val Lys Arg Pro Ala Ala Thr Lys Lys Ala Gly Gln Ala Lys Lys Lys Lys Leu Asp) ([SEQ ID NO:15](#)); Dingwall, et al., Cell, 30:449-458, 1982 and Dingwall, et al., J. Cell Biol., 107:641-849; 1988). Numerous localization studies have demonstrated that NLSs incorporated in synthetic peptides or grafted onto reporter proteins not normally targeted to the cell nucleus cause these peptides and reporter proteins to be concentrated in the nucleus. See, for example, Dingwall, and Laskey, Ann. Rev. Cell Biol., 2:367-390, 1986; Bonnerot, et al., Proc. Natl. Acad. Sci. USA, 84:6795-6799, 1987; Galileo, et al., Proc. Natl. Acad. Sci. USA, 87:458-462, 1990.

Please replace paragraph [0243] with the following rewritten paragraph:

[0243] MRI contrast agents comprising MMP recognizable peptides can be synthesized as described below. The basic peptide sequence pro-met-ala-leu-trp-met-arg ([SEQ ID NO:4](#)) can serve as the starting point for synthesizing MMP recognizable peptides. This sequence is recognized by MMPs 7, with or without the attachment of a fluorescent label, suggesting that if the label is replaced with a contrast agent, the peptide can still be recognized (Netzel-Arnett, S.; Siang, Q.; Moore, W. G.; Mavre, M.; Birkedal-Hansen, H.; Wart, H. E. V. Biochem. 1993, 32, 6427-6432).

Please replace paragraph [0250] with the following rewritten paragraph:

[0250] arginine-methionine-tryptophan-leucine-DOTA (SEQ ID NO:16) (MJA156): Polystyrene based Wang resin containing an fmoc protected arginine-methionine-tryptophan-leucine (SEQ ID NO:16) chain (1.40 g, 0.436 mmol/g) was swelled in dichloromethane and then washed four times with dimethylformamide (DMF). The resin was treated twice with a solution of 20% piperidine in DMF for ten minutes. The resin was washed four times with DMF. In a separate vial DOTA(tris-t-bu ester) (0.698 g, 1.22 mmol), O-(7-azabenzotriazol-1-yl)-1,3,3-tetramethyluronium hexafluorophosphate (HATU), (0.455 g, 1.20 mmol), and DMF (5 mL) were combined and then diisopropylethylamine (0.532 mL, 3.05 mmol) was added. The resulting solution was added to the resin and bubbled with argon for two hours. The resin was then drained and rinsed four times with DMF. A solution of 81.5% TFA, 5% thioanisole, 5% phenol, 5% water, 2.5% ethanedithiol, and 1% triisopropylsilane was then added to the resin and the mixture was bubbled with argon for one hour then drained. The resin was then rinsed with TFA. The filtrate and rinse were combined and reduced in volume to ten milliliters. Forty milliliters of -20° C. MTBE was added to precipitate a white solid. The solid was washed three times with cold MTE, taken up in water and freeze dried to a white powder. The white powder was exposed to the TFA solution for two hours to deprotect the t-butyl esters, washed with cold MTBE as above and freeze dried to yield a white powder. Yield=0.040 g (6.6%). ¹H NMR (D2O): δ=0.8-4.0 (m, 48H), 4.1-4.7 (m, 4H), 7.1-7.6 (m, 511); ¹³C NMR (D₂O): δ=14.36, 21.31, 22.21, 24.56, 27.15, 27.72, 29.16, 30.48, 30.65, 39.93, 40.66, 49.77 (4s), 52.61, 54.41 (4s), 108.80, 111.98, 118.43, 119.48, 122.05, 124.34, 127.12, 136.13, 156.67, 170.44 (3s), 172.55, 173.06, 174.09, 174.92; MS Calcd for C₄₄H₇₀N₁₂O₁₂S [M+H]⁺: 991.5, found 991.6.

Please replace paragraph [020] with the following rewritten paragraph:

[0251] arginine-methionine-tryptophan-leucine-alanine-DOTA (SEQ ID NO:17) (MJA134): Polystyrene based Wang resin containing an fmoc protected arginine-methionine-tryptophan-leucine-alanine (SEQ ID NO:17) chain (1.00 g, 0.501 mmol/g) was swelled in dichloromethane and then washed four times with dimethylformamide (DMF). The resin was treated twice with a solution of 20% piperidine in DMF for ten minutes. The resin was washed four times with DMF. In a separate vial DOTA(tris-t-bu ester) (0.566 g, 1.00 mmol), O-(7-azabenzotriazol-1-yl)-1,3,3-tetramethyluronium hexafluorophosphate (HATU), (0.373 g, 0.982 mmol), and DMF (5 mL) were combined and then

diisopropylethylamine (0.436 mL, 2.51 mmol) was added. The resulting solution was added to the resin and bubbled with argon for two hours. The resin was then drained and rinsed four times with DMF. A solution of 81.5% TFA, 5% thioanisole, 5% phenol, 5% water, 2.5% ethanedithiol, and 1% triisopropylsilane was then added to the resin and the mixture was bubbled with argon for one hour then drained. The resin was then rinsed with TFA. The filtrate and rinse were combined and reduced in volume to ten milliliters. Forty milliliters of -20° C. MTBE was added to precipitate a white solid. The solid was washed three times with cold MTE, taken up in water and freeze dried to a white powder. The white powder was exposed to the TFA solution for seven hours to deprotect the t-butyl esters, washed with cold MTBE as above and freeze dried to yield a white powder. Yield=0.392 g (73.8%). ¹H NMR (D₂O): δ =0.8-4.0 (m, 51 H), 4.0-4.7 (m, 5H), 7.0-7.6 (m, 5H); ¹³C NMR (D₂O): δ =14.51, 16.23, 21.49, 22.39, 24.59, 26.24, 27.63, 27.99, 29.32, 30.74, 40.05, 40.70, 46.8-54.4 (12s), 108.89, 112.10, 118.46, 119.60, 122.33, 124.40, 127.12, 136.22, 156.60, 170.79 (5s), 172.58, 172.93, 174.22, 174.89; MS Calcd for C₄₇H₇₅N₁₃O₁₃S [M+H]⁺: 1062.5, found 1062.6.

[0252] arginine-methionine-tryptophan-leucine-alanine-methionine-DOTA (SEQ ID NO:18) (MJA157): Polystyrene based Wang resin containing an fmoc protected arginine-methionine-tryptophanleucine-alanine-methionine (SEQ ID NO:18) chain (1.20 g, 0.471 mmol/g) was swelled in dichloromethane and then washed four times with dimethylformamide (DMF). The resin was treated twice with a solution of 20% piperidine in DMF for ten minutes. The resin was washed four times with DMF. In a separate vial DOTA(tris-t-butyl ester) (0.638 g, 1.13 mmol), O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), (0.421 g, 1.11 mmol), and DMF (5 mL) were combined and then diisopropylethylamine (0.492 mL, 2.83 mmol) was added. The resulting solution was added to the resin and bubbled with argon for two hours. The resin was then drained and rinsed four times with DMF. A solution of 81.5% TFA, 5% thioanisole, 5% phenol, 5% water, 2.5% ethanedithiol, and 1% triisopropylsilane was then added to the resin and the mixture was bubbled with argon for one hour then drained. The resin was then rinsed with TFA. The filtrate and rinse were combined and reduced in volume to ten milliliters. Forty milliliters of -20° C. MTBE was added to precipitate a white solid. The solid was washed three times with cold MTE, taken up in water and freeze dried to a white powder. The white powder was exposed to the TFA solution for four hours to deprotect the t-butyl esters, washed with cold MTBE

as above and freeze dried to yield a white powder. Yield=0.496 g (73.6%). ^1H NMR (D_2O): δ =0.8-4.0 (m, 58H), 4.0-4.7 (m, 6H), 7.0-7.6 (m, 5H); ^{13}C NMR (D_2O): δ =14.41, 16.50, 21.11, 22.27, 24.55, 26.14, 26.59, 27.75, 29.19, 29.38, 30.43, 30.80, 39.68, 40.68, 49.70 (5s), 52.77 (9s), 108.46, 112.07, 114.48, 118.31, 119.62, 122.21, 124.39, 126.99, 136.24, 156.63, 172.70, 174.85 (9s); MS Calcd for $\text{C}_{52}\text{H}_{84}\text{N}_{14}\text{O}_{14}\text{S}_2$ $[\text{M}+\text{H}]^+$: 1193.6, found 1193.6.

[0253] arginine-methionine-tryptophan-leucine-alanine-methionine proline-DOTA (MJA098): Polystyrene based Wang resin containing an fmoc protected arginine-methionine-tryptophanleucine-alanine-methionine-prolin- e chain (0.969 g, 0.417 mmol/g) was swelled in dichloromethane and then washed four times with dimethylformamide (DMF). The resin was treated twice with a solution of 20% piperidine in DMF for ten minutes. The resin was washed four times with DMF. In a separate vial DOTA(tris-t-bu ester) (0.500 g, 0.885 mmol), O-(7azabenzotriazol-1-yl)-1,1,3,3-tetramethyluroniu hexafluorophosphate (HATU), (0.320 g, 0.841 mmol), and DMF (5 mL) were combined and then diisopropylethylamine (0.386 mL, 2.21 mmol) was added. The resulting solution was added to the resin and bubbled with argon for twelve hours. The resin was then drained and rinsed four times with DMF. A solution of 81.5% TFA, 5% thioanisole, 5% phenol, 5% water, 2.5% ethanedithiol, and 1% triisopropylsilane was then added to the resin and the mixture was bubbled with argon for one hour then drained. The resin was then rinsed with TFA. The filtrate and rinse were combined and reduced in volume to ten milliliters. Forty milliliters of -20.degree. C. MTBE was added to precipitate a white solid. The solid was washed three times with cold MTE, taken up in water and freeze dried to a white powder. The white powder was exposed to the TFA solution for seven hours to deprotect the t-butyl esters, washed with cold MTBE as above and freeze dried to yield a white powder. Yield=0.278 g (53.2%). ^1H NMR (D_2O): δ =0.8-4.0 (m, 66H), 4.0-4.6 (m, 7H), 7.0-7.6 (m, 5H); ^{13}C NMR (D_2O): δ =14.44, 16.58, 21.11, 22.33, 24.62, 26.18, 27.51, 27.80, 29.41, 29.73, 30.45, 30.83, 39.75, 40.71, 46.97, 49.74, 50.0 (4s), 52.57, 52.82, 53.00, 53.20, 53.6 (3s), 54.48, 108.52, 112.10, 118.38, 119.66, 122.2, 124.44, 127.02, 136.28, 156.64, 172.7-17.9 (11s); MS Calcd for $\text{C}_{57}\text{H}_{91}\text{N}_{15}\text{O}_{15}\text{S}_2$ $[\text{M}+\text{H}]^+$: 1290.6, found 1290.6.

Please insert the 5-page text entitled "SEQUENCE LISTING" immediately preceding the claims.